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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/643,982	08/20/2003	Dov Zipori	85189-5000	5156

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EXAMINER	
BELYAVSKYI, MICHAIL A	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 10/24/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/643,982	ZIPORI ET AL.	
	Examiner	Art Unit	
	Michail A. Belyavskyi	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 August 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 4-27* is/are pending in the application.

4a) Of the above claim(s) *12-26* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,5-11 and 27* is/are rejected.

7)☒ Claim(s) *4* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

RESPONSE TO APPLICANT'S AMENDMENT

1. Applicant's amendment, filed 08/30/06 is acknowledged.

Claims 1, 4-27 are pending.

Claims 12-26 stand withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b) as being drawn to a nonelected invention.

Claims 1, 4-11 and 27 reads on an isolated polypeptide consisting of a transcript of an Ig μ heavy chain gene, the polynucleotide lacking V region sequence and consisting of a constant domain and joining region sequences and a 5' intronic J sequence upstream of the J region sequence including an in-frame methionine codon are under consideration in the instant application.

In view of the amendment, filed 08/30/06 the following rejections remain:

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 1, 5-11 and 27 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated polynucleotide consisting a truncated μ heavy chain of SEQ ID NOs: 1, 3, 4, 5 and 6 or encoding a peptide consisting of SEQ ID NO:2 ; an antisense DNA molecule to said polynucleotides ; an expression vector comprising said polynucleotides and a host cell comprising said vector does not reasonably provide enablement for: (i) any isolated polypeptide consisting of a transcript of an Ig μ heavy gene, the polynucleotide lacking V region sequence and consisting a constant domain and joining region sequences and a 5' intronic J sequence upstream of the J region sequence including an in-frame methionine codon, claimed in claimed in claims 1; or (ii) the polynucleotide encoding a peptide comprising SEQ ID NO:2, claimed in claim 5; or (iii) any antisense DNA molecule to said polynucleotides, claimed in claims 6-7; or (iv) any expression vector, comprising said polynucleotides, as claimed in claims 8-9 and 27; or (v) any host cells comprising said vector, claimed in claims 10-11 for the same reasons set forth in the previous Office Action, mailed on 05/30/06.

Applicant's arguments, filed 08/30/06 have been fully considered, but have not been found convincing.

Applicant asserts that: (i) amended claims now recites an isolated polypeptide consisting of a truncated μ heavy chain of SEQ ID NOs: 1, 3, 4, 5 and 6 or encoding a peptide consisting of SEQ ID NO:2; (ii) Applicant have provided a variety of examples of transcripts consisting of Ig heavy constant and joining region sequences and 5'intronic J sequence upstream of the J region to enable one skill in the art to identify the number of the representative compounds falling within the scope of the instant claims; (iii) A Declaration under 37 CFR 1.132 by Dr. Zipori provide evidences that as presently claimed the invention is enabling.

Contrary to Applicant's assertion it is noted that amended claims still recited the open-ended "comprising" language. For example, claims 5 and 27 still recited a polynucleotide encoding a peptide comprising SEQ ID NO:2 and claims 7 and 9 still recited polynucleotide comprising SEQ ID NO:1.

With regards to Applicant's statement that "Applicant have provided a variety of examples of transcripts consisting of Ig heavy constant and joining region sequences and 5'intronic J sequence upstream of the J region"

As has been stated previously, applicant discloses a novel polynucleotide consisting of a truncated μ heavy chain of SEQ ID NOs: 1,3, 4, 5 and 6 or encoding a peptide consisting of SEQ ID NO:2 ; an antisense DNA molecule to said polynucleotides ; an expression vector comprising said polynucleotides and a host cell comprising said vector in the instant application (see overlapping pages 7-11 and Example 2 of the instant Application). Applicant disclosed that transcripts of said novel polynucleotides are involved in regulation of stem cell growth and differentiation (see pages 12 and 14 in particular). Applicant only disclosed that "it is anticipated that additional molecular variants of the Ig superfamily will be transcribed and expressed on mesemchymal and/or endothelial cells" (see page 18 in particular)

Applicant has not taught how to make and/or use : (i) any isolated polypeptide consisting of a transcript of an Ig μ heavy gene, the polynucleotide lacking V region sequence and consisting a constant domain and joining region sequences and a 5' intronic J sequence upstream of the J region sequence including an in-frame methionine codon, claimed in claimed in claims 1; or (ii) the polynucleotide encoding a peptide comprising SEQ ID NO:2, claimed in claim 5; or (iii) any antisense DNA molecule to said polynucleotides, claimed in claims 6-7; or (iv) any expression vector, comprising said polynucleotides, as claimed in claims 8-9 and 27; or (v) any host cells comprising said vector, claimed in claims 10-11. The structural and functional characteristics of said nucleic acid molecules are not defined in the claim.

Since the instant fact pattern fails to indicate that representative number of structurally related compounds is disclosed, the artisan would not know the identity of a reasonable number of representative compounds falling within the scope of the instant claims and consequently would

not know how to make them. An assay for *finding* a product is not equivalent to a positive recitation of *how to make* a product.

With regards to Applicants comments that "A Declaration under 37 CFR 1.132 by Dr. Zipori provide evidences that as presently claimed the invention is enabling".

It is the Examiner position that said declaration corroborate the examiner enablement rejection. In said declaration, Dr. Zipori stated that only very specific truncated form of μ heavy chain , designated as stro-μ , when expressed in human 293T cells results in G1 cell cycle arrest. As has been stated previously, it is the Examiner position that the instant claims only enabling for a specific truncated form of μ heavy chain consisting of SEQ ID NOs: 1, 3, 4, 5 and 6 or encoding a peptide consisting of SEQ ID NO:2. Transcripts of said novel polynucleotides have been shown to be involved in regulation of stem cell growth and differentiation.

"Comprising" is considered open-ended claim language and expand an isolated polynucleotide to include additional non disclosed nucleic acids sequences outside of the specified sequences. The disclosure of a novel polynucleotide consisting of a truncated μ heavy chain of SEQ ID NOs: 1,3, 4, 5 and 6 or encoding a peptide consisting of SEQ ID NO:2 that are involved in regulation of stem cell growth and differentiation cannot support the entire genus of : (i) any isolated polypeptide comprising a transcript of an Ig gene, the polynucleotide lacking V region sequence and comprising a constant domain and joining region sequences and a 5' intronic J sequence upstream of the J region sequence including an in-frame methionine codon, claimed in claimed in claims 1-3; or (ii) comprising a truncated μ heavy chain of SEQ ID NOs: 1,3, 4, 5 and 6, claimed in claims 4-6; or (iii) any antisense DNA molecule to said polynucleotides, claimed in claims 6-7; or (iv) any expression vector, comprising said polynucleotides, as claimed in claims 8-9; or (v) any host cells comprising said vector, claimed in claims 10-11.

There does not appear to be sufficient guidance in the specification as filed as to how the skilled artisan would make the various polynucleic acids recited in the instant claims. A person of skill in the art would not know which sequences are essential and which sequences are non-essential for the function of said polynucleotides i.e. for regulation of stem cell growth and differentiation.

Applicant is relying upon certain biological activities and the disclosure of a limited species to support an entire genus. It is well known that minor structural differences among even structurally related compounds or compositions can result in substantially different biology, expression, and pharmacology of proteins. Therefore, structurally unrelated: (i) any isolated polypeptide consisting of a transcript of an Ig μ heavy gene, the polynucleotide lacking V region sequence and consisting a constant domain and joining region sequences and a 5' intronic J sequence upstream of the J region sequence including an in-frame methionine codon, claimed in claimed in claims 1; or (ii) the polynucleotide encoding a peptide comprising SEQ ID NO:2, claimed in claim 5; or (iii) any antisense DNA molecule to said polynucleotides, claimed in

claims 6-7; or (iv) any expression vector, comprising said polynucleotides, as claimed in claims 8-9 and 27; or (v) any host cells comprising said vector, claimed in claims 10-11 encompassed by the claimed invention would be expected to have greater differences in their activities.

Since the nucleic acid sequence of a polynucleotide determines its protein coding properties, predictability of which changes can be tolerated in a polynucleotides nucleic acid sequence and still retain similar functions and properties requires a knowledge of, and guidance with regard to which nucleic acids within the full-length nucleotide sequence, if any, are tolerant of modification and which are conserved or less tolerant to modification, and detailed knowledge of the ways in which the product's structure relates to its functional usefulness. Because there is no guidance in the specification as to which amino acid sequence within the amino acid sequence of SEQ ID NO: 2, which is encoded by polypeptide consisting of SEQ ID NO:1 that after substitution, deletion or insertion will retain the same function, i.e. regulate stem cell growth and differentiation it is unpredictable to determine which polynucleotide consisting of a transcript of an Ig gene, the polynucleotide lacking V region sequence and consisting of a constant domain and joining region sequences and a 5' intronic J sequence upstream of the J region sequence including an in-frame methionine codon; or (ii) the polynucleotide encoding a peptide comprising SEQ ID NO:2, will have similar function . Since the structure associated with functions of any polynucleotide mentioned above are not disclosed, predicting which polynucleotide consisting of a transcript of an Ig gene, the polynucleotide lacking V region sequence and consisting of a constant domain and joining region sequences and a 5' intronic J sequence upstream of the J region sequence including an in-frame methionine codon; or (ii) the polynucleotide encoding a peptide comprising SEQ ID NO:2, will have the ability to regulate or modulate growth /differentiation of stem cells is well outside the realm of routine experimentation.

Reasonable correlation must exist between the scope of the claim and the scope of enablement set forth. Without sufficient guidance, the changes which can be made in the instantly recited any isolated polynucleotide sequences and still maintained the functional properties of polynucleotide consisting of a truncated μ heavy chain of SEQ ID NOs: 1,3, 4, 5 and 6 or encoding a peptide consisting of SEQ ID NO:2 is unpredictable, as is the identity of which fragments would encode a functional polypeptide since the amino acids encoding a particular functional activity do not appear to have been identified; thus the experimentation left to those skilled in the art is unnecessary, improperly, extensive and undue.

Thus, Applicant has not provided sufficient guidance to enable one skill in the art to make and use any isolated polypeptide consisting of a transcript of an Ig μ heavy gene, the polynucleotide lacking V region sequence and consisting a constant domain and joining region sequences and a 5' intronic J sequence upstream of the J region sequence including an in-frame methionine codon, claimed in claimed in claims 1; or (ii) the polynucleotide encoding a peptide comprising SEQ ID NO:2, claimed in claim 5; or (iii) any antisense DNA molecule to said polynucleotides,

claimed in claims 6-7; or (iv) any expression vector, comprising said polynucleotides, as claimed in claims 8-9 and 27; or (v) any host cells comprising said vector, claimed in claims 10-11 in the manner reasonably correlated with the scope of the claims. The scope of the claims must bear a reasonable correlation with the scope of enablement. *In re Fisher*, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute.

In view of the quantity of experimentation necessary, the unpredictability of the art, the lack of sufficient guidance in the specification, the limited working examples, and the limited amount of direction provided given the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

4. Claims 1, 5-11 and 27 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant is in possession of : an isolated polynucleotide consisting a truncated μ heavy chain of SEQ ID NOs: 1,3, 4, 5 and 6 or encoding a peptide consisting of SEQ ID NO:2 ; an antisense DNA molecule to said polynucleotides ; an expression vector comprising said polynucleotides and a host cell comprising said vector

Applicant is not in possession of : (i) any isolated polypeptide consisting of a transcript of an Ig μ heavy gene, the polynucleotide lacking V region sequence and consisting of a constant domain and joining region sequences and a 5' intronic J sequence upstream of the J region sequence including an in-frame methionine codon, claimed in claimed in claims 1; or (ii) the polynucleotide encoding a peptide comprising SEQ ID NO:2, claimed in claim 5; or (iii) any antisense DNA molecule to said polynucleotides, claimed in claims 6-7; or (iv) any expression vector, comprising said polynucleotides, as claimed in claims 8-9 and 27; or (v) any host cells comprising said vector, claimed in claims 10-11.

Applicant's arguments, filed 08/30/06 have been fully considered, but have not been found convincing.

Applicant asserts that the instant specification describe a genus of polynucleotide sequences consisting of a constant domain and joining region sequences and a 5' intronic J sequence upstream of the J region sequence including an in-frame methionine codon, by recitation of polypeptide sequences of SEQ ID NO: 1,3,4, 5 and 6.

It is noted that SEQ ID N)s 1, 3, 4 and 5 are not polypeptide but polynucleotide sequences.

However, the issue raised in the previous Office Action was that the claimed invention is drawn to a genus of an isolated polynucleotide, however, structural identifying characteristics of the genus are not disclosed. There is no evidence that there is any *per se* structure/function relationship between the disclosed isolated polynucleotide consisting a truncated μ heavy chain of SEQ ID NOs: 1,3, 4, 5 and 6 or encoding a peptide consisting of SEQ ID NO:2 that are involved in the regulation of stem cell growth and differentiation and any isolated polypeptide consisting of a transcript of an Ig μ heavy gene, the polynucleotide lacking V region sequence and consisting of a constant domain and joining region sequences and a 5' intronic J sequence upstream of the J region sequence including an in-frame methionine codon.

A description of what a material does rather than of what it is, usually does not suffice. The patent does not more than describe the desired function of the compound called for and contains no information by which a person of ordinary skill in the art would understand that the inventors possessed the claimed invention. At best, it simply indicates that one should run tests on a wide spectrum of compounds in the hope that at least one of them will work. Inadequate written description that merely identifies a plan to accomplish an intended result "is an attempt to preempt the future before it has arrived" *Fiers v. Revel*, 984 F.2d 1164,1171 9Fed.Cir. 1993).

Applicant has disclosed a limited number of species; therefore, the skilled artisan cannot envision all the contemplated polynucleotide sequence possibilities recited in the instant claims. Consequently, conception in either case cannot be achieved until a representative description of the structural and functional properties of the claimed invention has occurred, regardless of the complexity or simplicity of the method. Adequate written description requires more than a mere statement that it is part of the invention. The sequences themselves are required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993).

A description of a genus of polynucleotide sequences may be achieved by means of a recitation of a representative number of polypeptide sequences, defined by amino acid sequence, falling within the scope of the genus, or of a recitation of structural features common to the genus, which features constitute a substantial portion of the genus. Regents of the University of California v. Eli Lilly&Co., 119F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997).

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.). Consequently, Applicant was not in possession of the instant claimed invention. See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.

Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

5. Claim 4 is objected to as being dependent upon a rejected base claim 1, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

6. No claim is allowed.

7. **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michail Belyavskyi whose telephone number is 571/ 272-0840 The examiner can normally be reached Monday through Friday from 9:00 AM to 5:30 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571/ 272-0841 .

The fax number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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